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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/689,469	10/12/2000	Anne Marie Schmidt	0575/55424-A-PCT-US/JPW/J	7726

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05/07/2002

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EXAMINER

YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 05/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/689,469

Applicant(s)

SCHMIDT ET AL.

Examiner

Christopher H Yaen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 February 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 42-81 is/are pending in the application.
- 4a) Of the above claim(s) 42-56 and 79-81 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 57-78 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7. 6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group III in Paper No. 10 is acknowledged. The traversal is on the ground(s) that the restriction is improper and illegal. This is not found persuasive because the invention of groups I, II and IV are drawn to separate and distinct inventions that all have unique outcomes, purposes and methodological steps that require a distinct search of the prior art. In addition, the inventions of group I, II, and IV are classified in distinct classes and subclasses, therefore warranting the separation of the invention. The requirement is still deemed proper and is therefore made **FINAL**.

Information Disclosure Statement

2. The information disclosure statement filed 8/31/2001 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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4. Claims 74-75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). The terms "*cadherin*" and "*integrin*" in claim 74 and 75 are used by the claims to mean "*extracellular matrix molecule*" while the accepted definitions of the terms are receptors. It is also noted that claim 74 is an improper Markush group that have species that are not related to the genus of extracellular matrix molecules.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 57-78 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a soluble RAGE molecules as an agent which inhibits tumor invasion, does not reasonably provide enablement for agents in general or any agent other than soluble RAGE. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 57-78 are drawn to a method of identifying agents that inhibit tumor invasion by admixing tumor cells with an agent, wherein a decrease in spreading indicates an agent that is able to inhibit invasion of tumor cells. Although the claims are

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enabled for the use of a soluble form of RAGE as an agent to inhibit invasion of a tumor cells, the instant specification has not enabled the use of other agents (polypeptides, peptidomimetics, nucleic acids, carbohydrates, lipid, antibody or fragments, or small molecules). Because the breadth of the claims encompass agents that are not described in the specification in such a way that would allow one of skill in the art to practice the claimed invention, the instant specification invites one of skill in the art to experiment.

The factors which must be considered in determining undue experimentation are set forth in In re Wands 8 USPQ2d 1400. The factors include: (1) quantity of experimentation, (2) the amount of guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the predictability of the art and, (7) breadth of the claims.

With regards to factors one and two cited above, the quantity of experimentation needed to determine which agents are able to inhibit invasion of tumor cells and the amount of decrease in cellular spreading which is needed to indicate that an agent is a potential candidate for inhibiting tumor invasion, is high because the instant specification has not adequately disclosed specific methodological steps, for each agent intended to be identified, which must be followed in order to reach the desired end point.

With regards to factors four, five, and six cited above, it is noted there is a great deal of unpredictability associated with the identification of agents/drugs that are effective for the treatment or prevention of cancer. As evidenced by Gura *et al.* methods for identifying potential new cancer drugs can at times be difficult and

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ineffective (Science 1997 Nov 7; 278:1041-1042). The instant specification fails to provide a specific methodological procedure for the identification of such agents, specifically, the agents mentioned in the instant application. For example, one of ordinary skill would be forced into undue experimentation to begin to look for peptides and analogs, peptidomimetics, inorganic and organic compounds, antibody or fragments thereof, and small molecules, because one of ordinary skill would find it difficult to even begin to search the countless number of potential candidates that could be used to obtain the desired end point.

With regards to factors, three and seven cited above, it is noted that the instant specification provides examples of how to use one particular agent, namely soluble RAGE, but does not provide examples or evidence that other agents can be identified and what it is that is that one of skill in the art is to look for in the identification of agents which inhibit invasion of tumors. The breadth of the claims encompass the identification of any agent that is able to inhibit invasion, while the specification has only enabled the use and identification of a soluble form of RAGE. It is noted that Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves, see In re Gardner et al. 166 USPQ 138 (CCPA 1970).

8. Claims 57 and 61 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The steps or protocol needed to identify agents that are nucleic acids using the steps of claim 57 are critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re*

Mayhew, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). The instant application claims to identify agents that are able to inhibit invasion of tumor cells. An agent named in claim 61 fails to be used in the steps outlined in claim 57, wherein the steps seem to be referring to methodological steps for the identification of protein based or chemical agents, and not for nucleic acid molecules. The instant application is silent in this regard, because the specification has not disclosed how a protein based assay for the identification of agents can be used as a method for the identification of nucleic acid agents.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 57-61, 66, 71-72, 76-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hori *et al.* (J. Biol. Chem. 1995; 270(43):25752-25761) in view of Miki S *et al.* (Biochem Biophys Res Commun 1993 Oct 29;196(2):984-9). Claims 57-61, 66, 71-72, 76-78 are drawn to a method of identifying an agent, wherein the agent is soluble RAGE, that is able to inhibit invasion of tumor cells.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Hori *et al.* disclose of a method of inhibiting the binding of amphoterin to RAGE by incubating an agent, sRAGE or soluble RAGE, to plates coated with amphoterin. Hori *et al.* used this method to identify the amount of cell growth was inhibited by sRAGE. Hori *et al.* further disclose of the involvement of amphoterin interaction with RAGE and that an important mechanism for the invasiveness of neoplastic lesions is dependent on the interaction of amphoterin with RAGE (pg 25760 column 2). Hori *et al.* however do not disclose of tumor association with RAGE. Miki S *et al.* however, do disclose of RAGE expression in cancer cells, and further disclose that RAGE is associated with cellular growth.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to develop a method of identifying an agent, namely a soluble

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RAGE, that was able inhibit cellular invasion, because the prior art provides sufficient motivation to practice the invention as claimed. The suggestion or motivation for doing what the applicant has claimed is that it was already known that sRAGE was available and that it was able to inhibit cellular growth (Hori *et al.*). It was also known that RAGE and amphoterin may have been an important interaction in neoplastic events (Hori *et al.*). In addition, it was also known that cancerous cells express RAGE (Miki *et al.*) and that since cancerous cells express such receptors, an agent that is able to inhibit normal cell growth may indeed be able to inhibit cancerous cells from growing/spreading and hence invading. Therefore it would have been *prima facie* obvious at the time of the invention to discern of a method to identify agents that are able to inhibit invasion of tumor cells using amphoterin and sRAGE.

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Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-

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308-4242 for regular communications and 703-305-3014 for After Final

communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
May 2, 2002


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